UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/719,758	01/04/2002	Fabienne Parker	ST98017 A	4189

5487 7590 07/17/2003

ROSS J. OEHLER
AVENTIS PHARMACEUTICALS INC.
ROUTE 202-206
MAIL CODE: D303A
BRIDGEWATER, NJ 08807

EXAMINER	
HELMS, LARRY RONALD	
ART UNIT	**PAPER NUMBER**
1642	15

DATE MAILED: 07/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/719,758	PARKER ET AL.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *5,6,10 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-9 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: NOTICE TO COMPLY

LM

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 1-4, 7, 8-9 and 12, in Paper No. 13 is acknowledged. The traversal is on the ground(s) that "the method of Schauffhausen does not enable one to make the antibodies of the invention with a reasonable expectation of success" and the method is unpredictable 9see page 2-3 of response). This is not persuasive. Applicant has provided no evidence to establish why the requirement for restriction is improper. In addition the method of Schauffhausen teach many antibodies to many peptides and as such one would conclude that one skill in the art could produce an antibody with the methods of Schauffhausen to the polypeptide of Parker. The cited locations in the reference are only considerations in choosing a peptide and Schauffhausen specifically teach "The production of antibodies to small peptides is now common laboratory practice" (see page 355). Thus there would be a reasonable expectation of success. Moreover, clearly different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is made **FINAL**.

2. Claim 10 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Applicant timely traversed the restriction (election) requirement in Paper No. 13.

NOTE: Claims 5-6 and 11 are also withdrawn as being not included in the restriction requirement as directed to non-statutory subject matter (see restriction requirement).

3. Claims 1-4, 7, 8-9, and 12 are under examination.

Sequence Requirements

4. Although a proper search could be performed on the claims, This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2) **See page 37-39 and Figure 4 for the G3BP2 protein**, for example. However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Any questions regarding compliance with the sequence rules requirements specifically should be directed to the departments listed at the bottom of the Notice to Comply.

APPLICANT IS GIVEN THE TIME ALOTTED IN THIS LETTER WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.R.F. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-4, 7-9, and 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly dawn to an antibody that is directed against the G3BP protein and is capable of inducing apoptosis in tumor cells. The specification only teaches one protein that is SEQ ID NO:1 that is the G3BP protein and is expressed in tumor cells (see pages 3, Figure 2a and 2b). The specification does not disclose any other G3BP proteins that have the properties of SEQ ID NO:1 and are expressed in tumor cells. Thus, one skill in the art would conclude that the claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

7. Claims 4, 7-9 and 12 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

It is unclear if a cell line which produces an antibody having the exact chemical identity of Mab 1F1 is known and publicly available, or can be reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line; (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

For example, very different V_H chains (about 50% homologous) can combine with the same V_K chain to produce antibody-binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_K sequences to produce antibodies with very similar properties. The results indicate that divergent variable region sequences, both in and out of the complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. [FUNDAMENTAL IMMUNOLOGY 242 (William E. Paul, M.D. ed., 3d ed. 1993)]. Therefore, it would require undue experimentation to reproduce the claimed antibody species Mab 1F1.

Deposit of the hybridoma would satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See, 37 C.F.R. 1.801-1.809.

Applicant's referral to the deposit of G3B 1F1 1D1 as I-2038 on page 5 of the specification is an insufficient assurance that the required deposit has been made and all the conditions of 37 CFR 1.801-1.809 met.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit is not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-3, 7-8 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parker et al (Molecular and Cellular Biology 16:2561-2569, 1996, IDS #8) and further in view of Schaffhausen (Hybridoma Technology in the Biosciences and Medicine, PTO892, attach to #12) and Harlow et al (Antibodies, a laboratory manual,

Cold spring harbor laboratory, chapter 6 and 7, 1988) and as evidenced from the specification.

The claims recite a monoclonal antibody that binds G3BP and is capable of inducing apoptosis in tumor cells and wherein the antibody recognizes an epitope of 1-144, 1-172 of G3BP and a pharmaceutical composition comprising the antibody and a hybridoma producing the antibody and a kit comprising the antibody. For this rejection the intended use of the composition for therapy or for diagnosis is given no patentable weight.

Parker et al teach the G3BP protein and antibodies to the protein. Parker et al does not teach antibodies recognizing residues 1-144 or 1-72 of G3BP or hybridomas secreting such antibodies. These deficiencies are made up for in the teachings of Schaffhausen et al and Harlow et al.

Schaffhausen et al teach production of monoclonal antibodies by immunization of peptides and the peptides are very often sequences from the amino terminal of the protein which is less restrictive in its conformation and in a survey the majority of peptides used for immunization were longer than 15 residues (see page 362).

Harlow et al teach production of monoclonal antibodies and hybridomas producing such.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used peptides of the G3BP protein as taught by Parker et al for production of antibodies to the amino terminus as taught by

Schaffhausen and produce hybridomas secreting such antibodies as taught by Harlow et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used peptides of the G3BP protein as taught by Parker et al for production of antibodies to the amino terminus as taught by Schaffhausen and produce hybridomas secreting such antibodies as taught by Harlow et al because Parker et al teach the amino acid sequence of the G3BP protein and in view of Schaffhausen who teaches producing antibodies to the amino terminal of protein because of the less restricted conformation it would be obvious to produce antibodies to the amino terminus and as such it would be obvious that such an antibody would induce apoptosis as evidenced from the specification that residues 1-14 are a domain involved in apoptosis and these are at the amino terminus of the protein. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used peptides of the G3BP protein as taught by Parker et al for production of antibodies to the amino terminus as taught by Schaffhausen and produce hybridomas secreting such antibodies as taught by Harlow et al because Harlow et al teach the production of hybridomas and Harlow et al is evidence that it was routine to produce hybridomas secreting antibodies.

Although claim 12 recites a kit, no positive recitation of the kit ingredients/elements distinguishes the claim over the references. Therefore, the references read on the claimed kit. Further, it is a well-known convention in the art to place the recited elements in a kit for the advantages of convenience and economy

Thus, the claimed subject matter is considered obvious over the prior art, absent sufficient factual evidence to the contrary.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

10. Claims 1-3, 7-8 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duchesne et al (US Patent 5,886,150, 7/97) and further in view of Schaffhausen (Hybridoma Technology in the Biosciences and Medicine, PTO892, attach to #12) and as evidenced from the specification.

The claims have been described supra. For this rejection the intended use of the composition for therapy or for diagnosis is given no patentable weight.

Duchesne et al teach the G3BP protein and monoclonal antibodies and hybridomas producing antibodies. These deficiencies are made up for in the teachings of Schaffhausen et al and Harlow et al.

Schaffhausen et al teach production of monoclonal antibodies by immunization of peptides and the peptides are very often sequences from the amino terminal of the protein which is less restrictive in its conformation and in a survey the majority of peptides used for immunization were longer than 15 residues (see page 362).

Harlow et al teach production of monoclonal antibodies and hybridomas producing such.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used peptides of the G3BP protein as

taught by Duchesne et al for production of antibodies to the amino terminus as taught by Schaffhausen and produce hybridomas as taught by Duchesne et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used peptides of the G3BP protein as taught by Duchesne et al for production of antibodies to the amino terminus as taught by Schaffhausen and produce hybridomas secreting such antibodies as taught by Duchesne et al because Duchesne et al teach the amino acid sequence of the G3BP protein and in view of Schaffhausen who teaches producing antibodies to the amino terminal of protein because of the less restricted conformation it would be obvious to produce antibodies to the amino terminus and as such it would be obvious that such an antibody would induce apoptosis as evidenced from the specification that residues 1-14 are a domain involved in apoptosis and these are residues at the amino terminus of the protein.

Although claim 12 recites a kit, no positive recitation of the kit ingredients/elements distinguishes the claim over the references. Therefore, the references read on the claimed kit. Further, it is a well-known convention in the art to place the recited elements in a kit for the advantages of convenience and economy

Thus, the claimed subject matter is considered obvious over the prior art, absent sufficient factual evidence to the contrary.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879

Application No. 09/719758

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: _____

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE